REMARKS

Section 103 Rejections

Claims 1-3 and 5-7 are rejected under 35 U.S.C. Section 103(a) as being unpatentable over Qian et al., Effreth et al., Zheng et al., Venugopalan et al, and Li et al., and further in view of Crooks et al. This ground of rejection is respectfully traversed.

Antiviral effect of artemisinin as described by Qian, Efferth, Zhang and Venugopalan

The position of the Examiner is that artemisinins have known antiviral activity and are known to have immunomodulatory activity, and therefore it is obvious to someone skilled in the art to test whether artemisinins would be active against HCV. The prior art does not, however, teach that artemisinins have antiviral activity against HCV, nor that the immunomodulatory activity of artemisinins would have an effect on HCV.

The Examiner's conclusion is not supported by the teachings asserted. There are thousands and thousands of compounds known to have antiviral activity in cell culture assays, and many have broad spectrum activity. Those skilled in the art recognize, however, that a known antiviral agent active against one or more viruses other than HCV does not teach that it will be active against HCV. It is admitted that artemisinin and its derivatives are known to be active against several viruses, such as several members of the Herpesviridae family (e.g. HCMV, HSV, Epstein-Barr virus). Further, compounds are known that have either broad antiviral activity (for example, acyclovir and cidofovir which are active against a broad spectrum of DNA viruses) or a more narrow antiviral spectrum (for example, ganciclovir). However, none of these antivirals have been shown to have efficacy against BVDV or HCV. Simply stated, activity of a compound against a virus other than HCV has no correlation to activity against HCV. It is not obvious to select artemisinin out of these thousands and thousands of compounds to specifically target HCV.

Artemisinin augments cell-mediated immunity as described by Crooks and Qian

With respect to immunomodulators, while it is well established that alpha interferons are effective agents for the treatment of HCV infections in man, not all interferons have such activity, and non-interferon immunomodulators may or may not stimulate interferon levels, and may or may not have an immunomodulatory effect on HCV by some other non-interferon

immune pathway. To someone skilled in the art, an interferon would be considered as something to test for HCV activity if a non-immune deficient animal model were available. It would not be obvious to think that an immunomodulator other than an interferon would be active against HCV. Moreover, based on the life cycle of HCV in the liver, it is generally questioned in the art whether immunomodulators other than interferons would have HCV therapeutic utility.

This is seen from the Crooks reference, which infers that immunomodulators may be effective antiviral agents particularly for HCV or like viruses specifically due to the observation that the compositions in Crooks stimulate interferon alpha activity (column 20, line 18). In contrast, the article by Qian teaches that the immunomodulatory activity of the atrimisinin (qinghaosu) has a suppressive effect on humoral immunity while enhancing cell-mediated immunity. The Qian paper in no way demonstrates a cell-mediate immunomodulatory effect working through interferon, and the viral assay showing influenza activity has no way been demonstrated to work through immunomodulation. The teaching in the art is that not all immunomodulators will have an HCV effect, and may in fact, like interferon alpha, need to work through a different, specific mechanism to be effective. In addition, the cell-mediated immunity effects seen for qinghaosu are unexplained - there is no mechanistic insight into the immunomodulatory effect or whether the immunomodulatory pathways required for an HCV effect are involved. Those skilled in the art know that not all immunomodulators will have an effect on HCV and, the fact of the matter is that there is a general belief in the field that only interferons will work therapeutically for HCV. The activity of the present compounds against HCV is not made obvious by the prior art, but rather the prior art teaches away from the surprising activity discovered by the inventors of the subject application.

The Section 103(a) rejections of claims 1-3 and 5-7 should be reconsidered and withdrawn.

Accordingly, the purpose of the claimed invention is not taught nor suggested by the cited references, nor is there any suggestion or teaching which would lead one skilled in the relevant art to combine the references in a manner which would meet the purpose of the claimed invention. Because the cited references, whether considered alone, or in combination with one another, do not teach nor suggest the purpose of the claimed invention, Applicant respectfully

submits that the claimed invention, as amended, patentably distinguishes over the prior art, including the art cited merely of record.

Based on the foregoing, Applicant respectfully submits that its claims 1-3, and 5-7 are in condition for allowance at this time, patentably distinguishing over the cited prior art. Accordingly, reconsideration of the application and passage to allowance are respectfully solicited.

The Examiner is respectfully urged to call the undersigned attorney at (515) 288-2500 to discuss any remaining issues that may exist or arise.

Respectfully submitted,

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